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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/470,944	12/22/1999	Gerard Gundling	6653.US.01	6792

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EXAMINER
SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
1637	18

DATE MAILED: 05/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/470,944	Applicant(s) GUNDLING, GERARD	
	Examiner ALEXANDER SPIEGLER	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Sharon N. Thornton
SHARON N. THORNTON
PATENT ANALYST

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to Paper No. 17, filed on March 5th, 2002. Currently, claims 1-2 and 4-16 are pending. All arguments have been full considered and thoroughly reviewed, but are deemed not persuasive for the reasons which follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-2 and 4-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uematsu et al. (EP 0757106 A2, 1997), in view of Kim et al. (WO 92/18514), and further in view of Chomczynski (USPN 5,945,515).

Uematsu et al.

Uematsu et al. disclose a method for isolating a nucleic acid by mixing a metal oxide support, a material containing a nucleic acid, and a solution for extracting the nucleic acid

forming a sample solution, separating the metal oxide support to which the nucleic acid has been bonded from the sample solution, and eluting the nucleic acid from the magnetic carrier to which the nucleic acid has been bonded (pg. 3, ln. 42-45). Uematsu et al. further teach that the solution used in the extraction of the nucleic acid contains a buffer containing a chaotropic material, such as guanidine salts, potassium iodide, sodium thiocyanate, sodium isothiocyanate, and urea (pg. 5, ln. 54-56). Furthermore, the reference teaches that the buffer can be used in combination with Triton X-100, a known detergent, and Tris HCl buffer (pg. 5, ln.56 - pg.6 ln. 1). With respect to claim 5, the reference further teaches a wash step of an aqueous solution of about 70% ethanol, following the separation of the metal oxide support/nucleic acid complex from the sample solution (pg.5, 43-44). With respect to claim 6, Uematsu et al. teach that following the wash step the nucleic acid is then eluted form the metal oxide support, with a Tris-EDTA bufer (TE buffer), or sterilized water (pg. 5, ln. 45). With respect to claim 7, the reference further teaches the detection of the nucleic acid after eluting the nucleic acid from the metal oxide support (pg. 3, ln. 57 - pg. 4, ln. 6). With respect to claim 8, the reference further teaches the step of amplifying the eluted nucleic acid (pg. 4, ln. 8-9). With respect to claim 9 and 10, the reference teaches that the nucleic acid used is RNA or DNA, and is taken from a biological source (i.e. whole blood, urine) (pg. 2-3).

Uematsu et al. teach a kit for isolating nucleic acid comprising a metal oxide support and a solution for extracting the nucleic acid, which is composed of a chaotropic agent, a detergent, and an elution buffer comprising water (pg. 4, ln. 10-12).

With respect to claim 12, the reference teaches (pg. 14, ln. 34-35) the amplification of the nucleic acid without the removal of the elution buffer.

With respect to claims 13-14, Uematsu teaches the elution of the nucleic acid can be conducted in a solution having a low ionic strength (for example, sterilized water, which has a pH of 7.0) (pg. 6, ln. 8-9).

Uematsu fails to teach:

1) Immobilizing the nucleic acid by forming a bond between the nucleic acid and the metal oxide support.

2) A binding buffer further comprising an organic solvent, wherein the flashpoint of the binding buffer is greater than 130 degrees Fahrenheit or the use of a reducing agent.

Kim et al.

Kim teaches the purification of nucleic acids using metal oxide supports. Specifically, the reference teaches the bonding of nucleic acid directly to a metal oxide support material (pg. 7, ln. 11-25), which provides the advantage in that the bonded nucleic acids can be readily isolated (pg. 3, ln. 14-21), and provides the benefits of an optimal combination of such properties as recovery, relative purity, and biological activity of the recovered nucleic acid, as well as, versatility, cost, speed, simplicity, and ease of use (pg. 3, ln. 31-35).

The reference also teaches that any biological sample containing the desired nucleic acids (pg. 3, ln. 22-30). With respect to claims 15-16, Kim teaches the elution of a bound nucleic acid from a metal oxide support material using potassium phosphate (Example 5, pgs. 17-18). In particular, Kim teaches that 30mM potassium phosphate is effective to recover 86% of bound DNA (pg. 17).

Chomczynski

Chomczynski teaches a solution for isolation of RNA, DNA, and proteins from biological material, where the solution comprises a chaotropic agent, detergent, and organic solvent (col. 10, ln. 22-34). With respect to claim 3, Chomczynski teaches that the addition of substantially lower amounts of organic solvents are required to effect the precipitation of cellular components (col. 3, ln.65-68). With respect to claims 2 and 4, Chomczynski further teaches that the solution for the isolation of RNA, DNA, and proteins, also comprises a reducing agent (see abstract, and col. 4 ln. 4). Chomczynski teaches that the reducing agent facilitates denaturation of RNase by the chaotropes and aids in the isolation of undegraded RNA.

With respect to claims 1-2 and 4-10, 12-14:

In view of the teachings of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu so as to have performed the method of separating nucleic acids from a test sample through the bonding of the nucleic acid to a metal oxide support material, in order to have achieved the benefits stated by Kim of providing a more versatile, cost-effective, and more efficient means of separation.

In view of the teachings of Chomczynski, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Uematsu and Kim so as to have added an organic solvent to the binding buffer, in order to have achieved the benefit of effecting the precipitation of cellular components (which would be expected to have a flashpoint of greater than 130^0 F); and a reducing agent to the binding buffer in order to have

achieved the advantages stated by Chomczynski of enhancing the denaturation of RNase present in the sample, thereby improving the isolation of RNA from the sample.

With respect to claim 11, the references fail to teach a kit comprising, a metal oxide particle (which bonds with a nucleic acid), a binding buffer (comprising a chaotropic agent, detergent, and an elution buffer), wherein said binding buffer has a flashpoint of greater than 130^0 F. However, reagent kits for performing DNA isolation assays were conventional in the field of molecular biology at the time the invention was made. In particular, kits provide the advantage of pre-assembling the specific reagents required to perform an assay and ensure the quality and compatability of the reagents to be used in the assay. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged a metal oxide particle (which bonds with a nucleic acid), a binding buffer (comprising a chaotropic agent and detergent), and an elution buffer, in a kit for the expected benefits of convenience and cost-effectiveness for practioners of the art.

With respect to claims 15-16, in view of the teachings of Kim, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Uematsu et al. so as to have used an elution buffer which comprises potassium phosphate in place of TE buffer in order to have provided an equally effective means for eluting the nucleic acids and providing a suitable medium for storing the eluted nucleic acid.

Applicants Arguments

4. Applicants argue:

1) Chomcynski does not suggest that the buffer be used is suitable for use with metal oxide particle mediated capture of nucleic acids. RNA is precipitated by centrifugation for 8 minutes, and DNA was isolated by adding additional solvent and centrifugation.

2) There is no motivation for combining the buffers of Chomcynski with the other references.

Response to Applicants Arguments

5. Applicants arguments are not found to be persuasive for the following reasons:

1) It is noted that the teachings of Uematsu, Kim and Chomcynski are to be used in combination with each other. While Chomcynski fails to teach using the buffer of the invention with metal oxide particles, Chomcynski does teach the benefits of using the buffer (i.e. effecting the precipitation of cellular components, facilitates denaturation of RNase by the chaotropes and aids in the isolation of undegraded RNA, etc.). Therefore, Chomcynski is relied upon for the actual buffer, and its advantageous properties. Uematsu and Kim teach the benefits of isolating nucleic acids on metal oxide particles. Therefore, when combining the advantageous buffer of Chomcynski with the benefits of isolating nucleic acids on metal oxide particles, as taught by Uematsu and Kim, one of ordinary skill in the art would have been expected to have arrived at the present invention.

Applicants point out that the isolation of RNA and DNA is different than that of the instant invention. While Chomcynski may teach alternative methods for isolating nucleic acids, Chomcynski is not being relied upon for the actual isolation method steps, but the binding buffer. Uematsu and Kim are being relied uupon for the actual isolation method steps.

2) Applicants argue that there is no motivation for combining the buffers of Chomcynski with the other references. This argument is not convincing because the test of obviousness under 35 USC 103 is not express suggestion of the claimed invention in any or all of the references, but what references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them (In re Rosselet, 146 USPQ 183(CCPA 1965). The fact that Chomcynski does not itself teach a combination of the buffer with metal oxide particles only mitigates against using this reference as an anticipatory reference, not as evidence in reaching a conclusion of obviousness under 35 USC 103. For the purposes of combining references, those references need not explicitly suggest combining teachings much less specific references. As stated in Ex parte Levengood, 28 USPQ2d 1300, "In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*, preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, or in the form of generally available knowledge, that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention".

Indeed, motivation for combining the teachings of the various references need not be explicitly found in the references themselves, but may be provided by the examiner based on logic and sound scientific reasoning. In the instant case, the ordinary artisan would have been motivated to have modified the method of Uematsu and Kim so as to have added an organic

solvent to the binding buffer, in order to have achieved the benefit of effecting the precipitation of cellular components (which would be expected to have a flashpoint of greater than 130^0 F); and a reducing agent to the binding buffer in order to have achieved the advantages stated by Chomczynski of enhancing the denaturation of RNase present in the sample, thereby improving the isolation of RNA from the sample.

Conclusion

6. No claims are allowable.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
May 20, 2002

CARLA J. MYERS
PRIMARY EXAMINER